REMARKS/ARGUMENTS

Claims 1-14 are pending. Claims 1, 2, 4 and 8 have been withdrawn from consideration. Claims 3 and 5-7 are subject to examination. The Applicants submit that new Claims 9 and 10 also conform to the prior restriction and election requirement and should be examined. Examination of new Claims 11-14 is also requested, upon an indication of allowability for the elected species.

As requested, clearer versions of Figs. 3 and 4 are provided to show the relative transcription differences obtained by the use of different primer pairs. Editorial revisions have been made to improve the clarity of the claims and independent Claim 3 and Claims 7 and 8 have been revised to refer to polynucleotide sequences consisting of particular defined sequences, such as SEQ ID NOS: 1-5 or 15-18. However, either the first or second oligonucleotide of these specific sequences further consists of an RNA polymerase promoter site. In view of the nature of the changes, the Applicants do not believe that any new matter has been added.

Election/Restriction

The restriction requirement has been made FINAL. The Applicants previously elected:

Restriction Group:	Group III, Claims 3 and 5-7;
Species of first oligonucleotide:	SEQ ID NO: 2;
Species of second oligonucleotide:	SEQ ID NO: 15.

Claim 3 is generic.

Objection—Claims

Claims 3 and 5 were objected to for minor informalities. The Applicants thank the examiner for indicating in the body of the Official Action (page 11) that these objections have been removed.

Rejection—35 U.S.C. § 112, second paragraph

Claims 3, 5, 6, 7, 9 and 10 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The Applicants believe these rejections are moot in view of the amendments above.

Rejection—35 U.S.C. § 103

Claims 3, 9 and 10 were rejected under 35 U.S.C. 103 as being unpatentable over Bekkaoui et al., U.S. Patent No. 6,136,533, in view of all of the following: Gilgen et al., Res. in Microbiol. 149:145; Calderwood et al., PNAS 84: 4364, and Buck et al., Biotechniques 27:528. Bekkaoui does not disclose or suggest a method for detecting VT1 RNA or disclose or suggest the oligonucleotides of SEQ ID NO: 2 or 15. The Official Action argues that Gilgen, Calderwood and Buck disclose amplification of the VT1 gene, disclose the full-length VT-1 gene sequence and expressly disclose the equivalence of different parts of a known nucleic acid sequence as primers. However, none of the cited prior art discloses or suggests selecting the particular oligonucleotides of the present invention.

Moreover, the Applicants disagree that the cited prior art would suggest or motivate one with ordinary skill in the art to apply the method of Bekkaoui to the detection of the VT1 gene, especially by using the specific oligonucleotides disclosed by the present specification.

These oligonucleotides as shown, for example, in Figure 3, provide superior RNA amplification results compared to other oligonucleotides. Thus, based on this data the Applicants respectfully disagree that all oligonucleotides are equivalents.

Presently, the invention has been examined as directed to Group III and as it reads on SEQ ID NOS: 2 and 15. The surprising and superior RNA amplification results provided by this combination of oligonucleotides are shown in Fig. 3 (see new clearer copy of Fig. 3 attached to this response), lanes 1-3 (lane 4 is a control). A clear copy of Figs. 3 and 4 is attached to this response. Fig. 3, lanes 1-3, show the RNA amplification obtained by using primers consisting of SEQ ID NOS: 2 and 15.

Lane	combination	Composition of combinations (a), (b) or (c)	VT-1 RNA Amount (copies/30µl)	Amount and clarity of banding pattern
1	(a)	5S (SEQ ID NO: 27) + 5F (SEQ ID NO: 36 = **SEQ ID NO: 15** + RNA Promoter Sequence) + 6R (**SEQ ID NO: 2**)	10^4	Heavy discrete banding
2	(a)		10^3	Heavy, discrete banding
3	(a)		10^3	Heavy, discrete banding
4	(a)		No RNA	
5	(b)	6S (SEQ ID NO: 28) + 6F (SEQ ID NO: 37 = SEQ ID NO: 16 + RNA Promoter Sequence) + 7R (SEQ ID NO: 26)	10^4	Moderate, discrete banding
6	(b)		10^3	Low banding
7	(b)		10^3	Low banding
8	(b)		No RNA	
9	(c)	6S (SEQ ID NO: 28) + 6F (SEQ ID NO: 37 = SEQ ID NO: 16 + RNA Promoter Sequence) + 8R (SEQ ID NO: 3)	10^4	Low, discrete banding
10	(c)		10^3	Low, discrete banding
11	(c)		10^3	Low, discrete banding
12	(c)		No RNA	

The superior amount and clarity of banding provided by selecting primers consisting of SEQ ID NOS: 2 and 15 (plus the RNA polymerase binding site) is clear from inspection of Fig. 3 as discussed in the Table above. Fig. 3, lands 1-3 (SEQ ID NOS: 2 and 15) shows heavy, clear and discrete banding in lane 1 (10^4 copies, amplification product length 141) as well as in lanes 2 and 3 which only use 10^3 copies of VT-1 RNA. Samples prepared with other oligonucleotide combinations (lanes 5-7, amplification length 166; lanes 9-11, amplification product length 346) show lower amounts of banding or less discrete banding. The Applicants submit that one with skill in the art would recognize that the intensity of banding corresponds to the amount of product present in the bands and that heavy, broad bands (e.g., in lanes 1-3) contain more product than less intense, narrower bands (e.g., lanes 9-11).

These data are described in the specification starting on page 12, line 16. As disclosed and as summarized in the Table above, Fig. 3 shows amplification reactions for VT1 RNA performed as described in Example 3. Lanes 1-4 use "combination (a)" where the oligonucleotides comprise SEQ ID NOS: 2 and 15--see "combination (a)" in Example 3. Compared to other oligonucleotide combinations such as (b), and (c) shown in Figs. 3 and 4, combination (a) provided clearer and more distinct banding. Thus, selection of a process using oligonucleotides consisting of SEQ ID NOS: 2 and 15 (plus the RNA polymerase binding site) provides a superior NASBA result compared to other oligonucleotide combinations.

While the selection of the combination of oligonucleotides of SEQ ID NOS: 2 and 15 provided the best results among those combinations in Table 3, other combinations, also provide superior results compared to selection of oliognucleotides which are excluded from the scope of the invention. Upon an indication of allowability for the elected species, the

Applicants request that examination be extended to the other oligonucleotide combinations encompassed by Claim 3 which is generic.

Since there is no suggestion in the prior art to combine the teachings of the cited documents, nor any suggestion of the superior results provided by selecting particular oligonucleotide sequences, the Applicants respectfully request that this rejection be withdrawn for the elected species.

In response to the remarks at the bottom of page 11 of the Official Action, the Applicants submit that (1) the copies of Figs. 3-4 herewith provided address the first concern regarding clarity and (2) point out that the superior properties of the combination comprising SEQ ID NO: 2 and SEQ ID NO: 15 are shown in the original disclosure in Fig. 3. Thus, there is no question that the Applicants were in possession of the invention as pertaining to the combination of SEQ ID NOS: 2 and 15 and the superior results flowing from this combination at the time of filing. (3) Claim 13 is directed to the specific combination of SEQ ID NO: 2 and 15. (4) Upon an indication of allowability for the elected species, the Applicants will further elaborate on the properties of the presently non-elected species directed to other combinations of the oligonucleotides in Claim 3.

Rejection—35 U.S.C. § 103

Claims 5-7 were rejected under 35 U.S.C. 103 as being unpatentable over Bekkaoui et al., U.S. Patent No. 6,136,533, in view of all of the following: Gilgen et al., Res. in Microbiol. 149:145; Calderwood et al., PNAS 84: 4364, and Buck et al., Biotechniques 27:528, as applied above, and further in view of Ishiguro et al., Nuc. Acid Res. 24:4992. The Applicants submit that this rejection may also be withdrawn in view of the arguments above. Ishiguro is cited for its disclosure of intercalator fluorescent dye and does not disclose or

suggest selecting the oligonucleotides of the present invention for use in a method for detecting VT1 RNA.

CONCLUSION

In view of the above amendments and remarks the Applicants submit that this application is now in condition for allowance. Early notification to that effect is earnestly solicited.

Respectfully submitted,

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